

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

Date of mailing (day/month/year) 27 February 2002 (27.02.02)	
International application No. PCT/AU01/00849	Applicant's or agent's file reference FP14725
International filing date (day/month/year) 13 July 2001 (13.07.01)	Priority date (day/month/year) 14 July 2000 (14.07.00)
Applicant BROWN, Tracey et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
 11 February 2002 (11.02.02)

☐ in a notice effecting later election filed with the International Bureau on:  
 \_\_\_\_\_

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  Cécile CHATEL (Fax 338.87.40)  Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

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From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

To:

DAVIES COLLISON CAVE  
Level 3  
303 Coronation Drive  
Milton, Queensland 4064  
AUSTRALIE

Date of mailing (day/month/year) 12 March 2002 (12.03.02)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference FP14725	
International application No. PCT/AU01/00849	International filing date (day/month/year) 13 July 2001 (13.07.01)

1. The following indications appeared on record concerning:		
<input type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input checked="" type="checkbox"/> the agent
<input type="checkbox"/> the common representative		
Name and Address GRIFFITH HACK Level 3 509 St Kilda Rd Melbourne, VIC 3004 Australia	State of Nationality	State of Residence
	Telephone No. +61 3 9243 8300	
	Facsimile No. +61 3 9243 8333	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input checked="" type="checkbox"/> the person	<input type="checkbox"/> the name	<input type="checkbox"/> the address
<input type="checkbox"/> the nationality	<input type="checkbox"/> the residence	
Name and Address DAVIES COLLISON CAVE Level 3 303 Coronation Drive Milton, Queensland 4064 Australia	State of Nationality	State of Residence
	Telephone No. +61 7 3368 2255	
	Facsimile No. +61 7 3368 2262	
	Teleprinter No.	
3. Further observations, if necessary: <b>A new agent has been appointed, as indicated in Box 2. The new agent's file reference should read: 2496346/EJH.</b>		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input checked="" type="checkbox"/> other: Former agent	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Eric LESOT (Fax 338.87.40)
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

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**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:

Tracey Brown

Richard Fox

Serial No.: 10/088,774

Filed: March 18, 2002

For: HYALURONAN AS A CYTOTOXIC  
AGENT, DRUG PRE-SENSITIZER AND  
CHEMO-SENSITIZER IN THE  
TREATMENT OF DISEASE

Group Art Unit: Unknown

Examiner: Unknown

Atty. Dkt. No.: DACO:002US

**EXPRESS MAIL MAILING LABEL**

NUMBER EV 119099469 US

DATE OF DEPOSIT March 13, 2003

**RESPONSE TO NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C.  
371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)**

**BOX PCT**

Commissioner for Patents

Washington, D.C. 20231

Sir:

In response to the Notification of Missing Requirements under 35 U.S.C. 371 in the United States Designated/Elected Office (DO/EO/US), dated January 17, 2003, there are enclosed herewith:

- (a) Declaration executed on behalf of Tracey Brown and Richard Fox;
- (b) A Power of Attorney on behalf of Meditech Research Limited;
- (c) Our check in the amount of \$130.00 to cover the surcharge for late filing; and
- (d) A copy of Notification of Missing Requirements under 35 U.S.C. 371 in the United States Designated/Elected Office (DO/EO/US).

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An Assignment to Meditech Research Limited and a check for \$40.00 are being filed under separate cover.

If the check is inadvertently omitted, or should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, or should an overpayment be included herein, the Commissioner is authorized to deduct or credit said fees from or to Fulbright & Jaworski Deposit Account No.: 50-1212/DACO:002US.

Please date stamp and return the accompanying postcard to evidence receipt of these documents.

Respectfully submitted,



REG. No. 37,257

Steven L. Highlander

Reg. No. 37,642

Attorney for Applicants

FULBRIGHT & JAWORSKI L.L.P.  
600 Congress Avenue, Suite 2400  
Austin, Texas 78701  
(512) 474-5201

Date: March 13, 2003

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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 14 NOV 2002

WIPO PCT

Applicant's or agent's file reference 2496346/EJH/aa1	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. <b>PCT/AU01/00849</b>	International Filing Date (day/month/year) 13 July 2001	Priority Date (day/month/year) 14 July 2000
International Patent Classification (IPC) or national classification and IPC <b>Int. Cl. <sup>7</sup> A61K 47/36, A61P 35/00</b>		
Applicant <b>MEDITECH RESEARCH LIMITED et al</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheet(s).

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 11 February 2002	Date of completion of the report 30 October 2002
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer  <b>G.R.PETERS</b> Telephone No. (02) 6283 2184

**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☐ the international application as originally filed.
- ☒ the description, pages **1-50**, as originally filed,  
pages , filed with the demand,  
pages , received on with the letter of
- ☒ the claims, pages , as originally filed,  
pages , as amended (together with any statement) under Article 19,  
pages , filed with the demand,  
pages **51-53**, received on **23 October 2002** with the letter of **23 October 2002**
- ☒ the drawings, pages **1/14-14/14**, as originally filed,  
pages , filed with the demand,  
pages , received on with the letter of
- ☐ the sequence listing part of the description:  
pages , as originally filed  
pages , filed with the demand  
pages , received on with the letter of

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

**4. ☐ The amendments have resulted in the cancellation of:**

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/fig.

**5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims 1-18	YES
	Claims	NO
Inventive step (IS)	Claims 1-18	YES
	Claims	NO
Industrial applicability (IA)	Claims 1-18	YES
	Claims	NO

**2. Citations and explanations (Rule 70.7)**Novelty (N) and Inventive Step (IS) claims 1-18.

The amended claims now emphasise that the invention is concerned with a method of treatment which prevents the formation of secondary neoplasms *via* proliferation of the cellular proliferative disease by pre-sensitising cells of the proliferative disease to the effect of a chemotherapeutic agent by the administration of Hyaluronic Acid and wherein the HA has a molecular weight of greater than or equal to 750,000 Daltons.

None of the citations describe such a method or use a HA having a molecular weight of greater than or equal to 750,000 Daltons. Consequently the present claims are regarded as being novel and inventive.

There is no doubt about Industrial Applicability of the claims.

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**CLAIMS**

1. A method of treatment of a cellular proliferative disease in a subject, said method comprising the steps of:-

- (i) pre-sensitizing cells of the proliferative disease to the effect of a chemotherapeutic agent by administering an effective amount of hyaluronan, optionally in combination with a pharmaceutical carrier, adjuvant or vehicle, wherein said hyaluronan has a molecular weight equal to or greater than 750,000; and
- (ii) subsequently administering a therapeutically effective amount of a chemotherapeutic agent, also optionally in combination with a pharmaceutical carrier, adjuvant or vehicle, provided that the said agent is not paclitaxel;

wherein the formation of secondary neoplasms *via* proliferation of the cellular proliferative disease is thereby prevented.

2. The method of Claim 1, wherein the cellular proliferative disease is selected from the group consisting of cancers of the breast, lung, prostate, kidney, skin, neural, ovary, uterus, liver, pancreas, epithelial, gastric, intestinal, exocrine, endocrine, lymphatic, haematopoietic system or head and neck tissue.

3. The method of Claim 1 or 2, wherein the subject is a mammal.

4. The method of Claim 3, wherein the mammal is selected from the group consisting of bovine, canine, equine, porcine and human.

5. The method of Claim 3, wherein the mammal is a human.

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6. The method of any one of Claims 1 to 5, wherein the chemotherapeutic agent is selected from the group consisting of carmustine (BCNU), chlorambucil (Leukeran), cisplatin (Platinol), Cytarabine, doxorubicin (Adriamycin), fluorouracil (5-FU), methotrexate (mexate), CPT111, etoposide, pliamycin (Mithracin) and taxanes.
7. The method of Claim 6, wherein the chemotherapeutic agent is fluorouracil (5-FU).
8. The method of Claim 6, wherein the chemotherapeutic agent is doxorubicin, also known as adriamycin.
9. The method of any one of Claims 1 to 8, wherein the administration is oral, topical or parenteral.
10. The method of Claim 9, wherein parenteral administration is by subcutaneous injection, by aerosol, by intravenous, intramuscular, intrathecal, intracranial or intrasternal injection, or by infusion techniques.
11. The method of any one of Claims 1 to 10, wherein the bio-availability of the chemotherapeutic agent is enhanced.
12. Use of hyaluronan and a chemotherapeutic agent in the preparation of a medicament for preventing the formation of secondary neoplasms *via* proliferation of the cellular proliferative disease in a subject, wherein said hyaluronan has a molecular weight equal to or greater than 750,000 and said agent is not paclitaxel, and wherein HA pre-sensitises cells of the proliferative disease to the effect of a chemotherapeutic agent.
13. The use of Claim 12, wherein the cellular proliferative disease is selected from the group consisting of cancers of the breast, lung, prostate, kidney, skin, neural, ovary, uterus, liver, pancreas, epithelial, gastric, intestinal, exocrine, endocrine, lymphatic, haematopoietic system or head and neck tissue.

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14. The use of any one of Claims 12 or 13, wherein the chemotherapeutic agent is selected from the group consisting of carmustine (BCNU), chlorambucil (Leukeran), cisplatin (Platinol), Cytarabine, doxorubicin (Adriamycin), fluorouracil (5-FU), methotrexate (mexate), CPT111, etoposide, pliamycin (Mithracin) and taxanes.
15. The use of Claim 14, wherein the chemotherapeutic agent is fluorouracil (5-FU).
16. The use of Claim 14, wherein the chemotherapeutic agent is doxorubicin, also known as adriamycin.
17. The use of any one of Claims 12 to 16, wherein the medicament is adapted for oral, topical or parenteral administration.
18. The use of Claim 17, wherein the medicament is adapted for parenteral administration by subcutaneous injection, by aerosol, by intravenous, intramuscular, intrathecal, intracranial or intrasternal injection, or by infusion techniques.

## PCT REQUEST

1/4

FP14725

Original (for SUBMISSION) - printed on 13.07.2001 01:34:19 PM

0	For receiving Office use only	
0-1	International Application No.	
0-2	International Filing Date	
0-3	Name of receiving Office and "PCT International Application"	
0-4	Form - PCT/RO/101 PCT Request	
0-4-1	Prepared using	PCT-EASY Version 2.92 (updated 01.03.2001)
0-5	Petition The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant)	Australian Patent Office (RO/AU)
0-7	Applicant's or agent's file reference	FP14725
I	Title of invention	HYALURONAN AS A CYTOTOXIC AGENT, DRUG PRE-SENSITIZER AND CHEMO-SENSITIZER IN THE TREATMENT OF DISEASE
II	Applicant	
II-1	This person is:	applicant only
II-2	Applicant for	all designated States except US
II-4	Name	MEDITECH RESEARCH LIMITED
II-5	Address:	Level 1 Sterling House 8 Parliament Place West Perth, Western Australia 6005 Australia
II-6	State of nationality	AU
II-7	State of residence	AU
III-1	Applicant and/or inventor	
III-1-1	This person is:	applicant and inventor
III-1-2	Applicant for	US only
III-1-4	Name (LAST, First)	BROWN, Tracey
III-1-5	Address:	23 Norwood Street Flemington, Victoria 3031 Australia
III-1-6	State of nationality	AU
III-1-7	State of residence	AU

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## PCT REQUEST

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III-2	<b>Applicant and/or inventor</b>	
III-2-1	This person is:	applicant and inventor
III-2-2	Applicant for	US only
III-2-4	Name (LAST, First)	FOX, Richard
III-2-5	Address:	171 Powlett Street East Melbourne, Victoria 3002 Australia
III-2-6	State of nationality	AU
III-2-7	State of residence	AU
IV-1	<b>Agent or common representative; or address for correspondence</b> The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	agent
IV-1-1	Name	GRIFFITH HACK
IV-1-2	Address:	Level 3 509 St Kilda Rd Melbourne, Victoria 3004 Australia
IV-1-3	Telephone No.	+61 3 9243 8300
IV-1-4	Facsimile No.	+ 61 3 9243 8333
IV-1-5	e-mail	ghmelb@griffithhack.com.au
V	<b>Designation of States</b>	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AP: GH GM KE LS MW MZ SD SL SZ TZ UG ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT EP: AT BE CH&LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR and any other State which is a Contracting State of the European Patent Convention and of the PCT OA: BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT
V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH&LI CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

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V-5	<b>Precautionary Designation Statement</b> In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	
V-6	<b>Exclusion(s) from precautionary designations</b>	NONE
VI-1	<b>Priority claim of earlier national application</b>	
VI-1-1	Filing date	14 July 2000 (14.07.2000)
VI-1-2	Number	PQ8795
VI-1-3	Country	AU
VI-2	<b>Priority document request</b> The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):	VI-1
VII-1	<b>International Searching Authority Chosen</b>	Australian Patent Office (ISA/AU)
VIII	<b>Declarations</b>	Number of declarations
VIII-1	Declaration as to the identity of the inventor	-
VIII-2	Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent	-
VIII-3	Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application	-
VIII-4	Declaration of inventorship (only for the purposes of the designation of the United States of America)	-
VIII-5	Declaration as to non-prejudicial disclosures or exceptions to lack of novelty	-
IX	<b>Check list</b>	number of sheets
IX-1	Request (including declaration sheets)	4
IX-2	Description	50
IX-3	Claims	2
IX-4	Abstract	1
IX-5	Drawings	14
IX-7	TOTAL	71
		electronic file(s) attached
		EZABST00.TXT


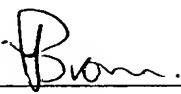

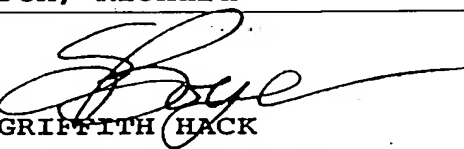
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## PCT REQUEST

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FP14725

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	Accompanying items	paper document(s) attached	electronic file(s) attached	
IX-8	Fee calculation sheet	✓	-	
IX-17	PCT-EASY diskette	-	Diskette	
IX-19	Figure of the drawings which should accompany the abstract	6		
IX-20	Language of filing of the international application	English		
X-1	Signature of applicant, agent or common representative			
X-1-1	Name			MEDITECH RESEARCH LIMITED
X-2	Signature of applicant, agent or common representative			
X-2-1	Name (LAST, First)			BROWN, Tracey
X-3	Signature of applicant, agent or common representative			
X-3-1	Name (LAST, First)			FOX, Richard
X-4	Signature of applicant, agent or common representative			
X-4-1	Name			GRIFFITH HACK
X-4-2	Name of signatory			Stuart James Boyer
X-4-3	Capacity			Patent Attorney

## FOR RECEIVING OFFICE USE ONLY

10-1	Date of actual receipt of the purported international application	
10-2	Drawings:	
10-2-1	Received	
10-2-2	Not received	
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application	
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)	
10-5	International Searching Authority	ISA/AU
10-6	Transmittal of search copy delayed until search fee is paid	

## FOR INTERNATIONAL BUREAU USE ONLY

11-1	Date of receipt of the record copy by the International Bureau	
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The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The name or two-letter code of that Authority may be indicated by the applicant on the line below.

IPEA/ \_\_\_\_\_

# PCT

## CHAPTER II

### DEMAND

Under Article 31 of the Patent Cooperation Treaty:

The Undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only

Identification of IPEA		Date of receipt of DEMAND
<b>Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION</b>		Applicant's or agent's file reference 2496346/EJH
International application No. PCT/AU01/00849	International filing date (day/month/year) 13 July 2001 (13-07-2001)	(Earliest) Priority date (day/month/year) 14 July 2000 (14-07-2000)
Title of invention Hyaluronan as a cytotoxic agent, drug pre-sensitizer and chemo-sensitizer in the treatment of disease		
<b>Box No. II APPLICANT(S)</b>		
Name and address: (Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country.) Meditech Research Limited Level 1 Sterling House 8 Parliament Place West Perth Western Australia 6005 Australia		Telephone No.:  Facsimile No.:  Email:.
State (that is, country) of nationality: Australia	State (that is, country) of residence: Australia	
Name and address: (Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country.) BROWN, Tracey 23 Norwood Street Flemington Victoria 3031 Australia		
State (that is, country) of nationality: Australia	State (that is, country) of residence: Australia	
Name and address: (Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country.) FOX, Richard 171 Powlett Street East Melbourne Victoria 3002 Australia		
State (that is, country) of nationality: Australia	State (that is, country) of residence: Australia	
<input checked="" type="checkbox"/> Further applicants are indicated on a continuation sheet.		

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**Box No. III AGENT OR COMMON REPRESENTATIVE: OR ADDRESS FOR CORRESPONDENCE**The following person is ☒ agent ☐ common representativeand ☐ has been appointed earlier and represents the applicant(s) also for international preliminary examination.☒ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.Name and address: *(Family name followed by given name; for a legal entity, full official designation.  
The address must include postal code and name of country.)*HUGHES, E John L  
ARGAET, Victor P  
THOMPSON, Paul MDAVIES COLLISON CAVE  
Level 3  
303 Coronation Drive  
Milton Queensland 4064  
Australia

Telephone No.:

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Facsimile No.:

+61-7-3368 2262

Email:

mail@davies.com.au

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.**Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION****Statement concerning amendments:\***

1. The applicant wishes the international preliminary examination to start on the basis of:

☐ the international application as originally filedthe description ☒ as originally filed☐ as amended under Article 34the claims ☐ as originally filed☒ as amended under Article 19 (together with any accompanying statement)☐ as amended under Article 34the drawings ☒ as originally filed☐ as amended under Article 342. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 2 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendment made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69. 1(d)). *This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

- Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

**Language for the purposes of international preliminary examination: English**☒ which is the language in which the international application was filed.☐ which is the language of a translation furnished for the purposes of international search.☐ which is the language of publication of the international application.☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.**Box No. V ELECTION OF STATES**The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

Excluding the following States which the applicant wishes not to elect:

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**Box No. VI CHECK LIST**

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- |    |   |   |  |        |
|----|---|---|--|--------|
| 1. | translation of international application                              | : |  | sheets |
| 2. | amendments under Article 34   | : |  | sheets |
| 3. | copy (or, where required, translation) of amendments under Article 19 | : |  | sheets |
| 4. | copy (or, where required, translation) of statement under Article 19  | : |  | sheets |
| 5. | letter  | : |  | sheets |
| 6. | other ( <i>specify</i> )  | : |  | sheets |

For International Preliminary Examining Authority use only

received not received

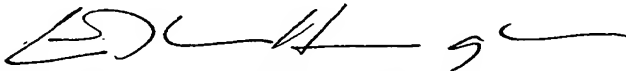
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
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The demand is also accompanied by the item(s) marked below:

- |                             |  |                             |   |
|-----------------------------|--|-----------------------------|---|
| 1. <input type="checkbox"/> | fee calculation sheet  | 4. <input type="checkbox"/> | statement explaining lack of signature                                  |
| 2. <input type="checkbox"/> | separate signed power of attorney                            | 5. <input type="checkbox"/> | nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> | copy of general power of attorney: reference number, if any: | 6. <input type="checkbox"/> | other ( <i>specify</i> ):   |

**Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE**

*Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).*



For and on behalf of the Applicants  
E John L HUGHES

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.

☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority dated as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority dated, the delay in arrival is EXCUSED pursuant to Rule 82.

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Demand received from IPEA on:

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GRIFFITH HACK

- 5 FEB 2002

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2 .....  
3 .....

PCT

# PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

To:

GRIFFITH HACK  
Level 3  
509 St Kilda Rd  
Melbourne, VIC 3004  
AUSTRALIE

NOTICE INFORMING THE APPLICANT OF THE  
COMMUNICATION OF THE INTERNATIONAL  
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

TRANSFERRED

DATE

14/1/2002

Date of mailing (day/month/year)

24 January 2002 (24.01.02)

Applicant's or agent's file reference

FP14725

IMPORTANT NOTICE

International application No.

PCT/AU01/00849

International filing date (day/month/year)

13 July 2001 (13.07.01)

Priority date (day/month/year)

14 July 2000 (14.07.00)

Applicant

MEDITECH RESEARCH LIMITED et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this notice:  
KP, KR, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OA, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this notice is a copy of the international application as published by the International Bureau on 24 January 2002 (24.01.02) under No. WO 02/05852

## REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination (at present, all PCT Contracting States are bound by Chapter II).

## REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and the PCT Applicant's Guide, Volume II.

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

J. Zahra

Telephone No. (41-22) 338.91.11

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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference FP14725	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/AU01/00849	International filing date (day/month/year) 13 July 2001	(Earliest) Priority Date (day/month/year) 14 July 2000
Applicant MEDITECH RESEARCH LIMITED et al		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (See Box II).

4. With regard to the **title**, ☒ the text is approved as submitted by the applicant. ✓  
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**, ☒ the text is approved as submitted by the applicant  
☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- ☐ as suggested by the applicant. ☒ None of the figures
- ☐ because the applicant failed to suggest a figure
- ☐ because this figure better characterizes the invention

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU01/00849

**A. CLASSIFICATION OF SUBJECT MATTER**Int. Cl. <sup>7</sup>: A61K 47/36, A61P 35/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

AU; IPC AS ABOVE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPAT, CAPLUS, MEDLINE; keywords: hyaluronic acid, Hyaluronan, HA, drug resist+, cancer, chemothera+

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 00/41730 A (MEDITECH RESEARCH LIMITED) 20 July 2000 Whole document	1-12
X	WO 99/02151 A (HYAL PHARMACEUTICAL CORPORATION) 21 January 1999. Whole document	2, 4-12
X	WO 97/40841 A (HYAL PHARMACEUTICAL CORPORATION) 6 November 1997. Whole document	2, 4-12

☒ Further documents are listed in the continuation of Box C ☒ See patent family annex

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

20 August 2001

Date of mailing of the international search report

22 August 2001

Name and mailing address of the ISA/AU

AUSTRALIAN PATENT OFFICE  
PO BOX 200, WODEN ACT 2606, AUSTRALIA  
E-mail address: pct@ipaustralia.gov.au  
Facsimile No. (02) 6285 3929

Authorized officer

G.R.PETERS

Telephone No : (02) 6283 2184

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU01/00849

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CA 2089621 A (NORPHARMCO INC) 17 August 1994. Whole document.	2, 4-12
X	WO 91/04058 A (NORPHARMCO INC) 4 April 1991. Whole document.	2, 4-12
X	Klein E.S et al, "Effects of hyaluronic acid on experimental tumor uptake of 5-fluorouracil" Regional Cancer Research (1994), 7 pp 163-164. Whole document.	2, 4-12

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INTERNATIONAL SEARCH REPORT  
Information on patent family members

International application No.  
PCT/AU01/00849

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
WO	00/41730	AU	24231/00				
WO	99/02151	AU	82031/98	CA	2208924		
WO	97/40841	AU	25644/97	CA	2175282		
WO	91/04058	AU	14850/97	AU	64330/90	AU	52274/93
		BR	2042034	CN	1051503	EP	445255
		EP	656213	US	5827834	US	5830882
		US	5985851	US	5990095	US	6022866
END OF ANNEX							

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